

-1696 TGTTTGCAATTAAAGTTTC
 -1680 ATAGATTATAAATTTGTAATGGAATCAACACCAAAATGCAAAATTAGAAAGAGAGCCCCACTTTTGCTCACCCAGTCACGTCCTTC
 -1600 CCATGTAAACCATAGAAACGTTGGGGTCTCTGTGTCTTTCTAGATCCACAGTCTTGCTCTCAGAACAGGCTAGCCACACACCACA
 -1520 GGCCTAGTGCCAGGACCCTATGGCCCTTTTAAAGCTCAGACTCCCTTCTGTGAACAGCAATATCCCCACAACCTTTGTACAA
 -1440 CATTTGGTGTCTCCCTGCAAGGGCTACAGAACTATTGTATACGAAAATGTTCAATTGACTTACACACAAGAGAACACAAAAT
 -1360 AAAAAATTAAATAATTAAATTAAATGTCTTTGAAAATGTACCATTTATTTTTACATTTGGGGTCAATAAGAAATTGTATTTACAC
 -1280 TTAAGAAATGCAATACAAATTGAAGATCAGATTTTCTCCCTTTGTGAGAAATTCTCAGTATGTTGTTGAATGACTTACCAAGAA
 -1200 ATCATAGCCAGTCATAAATTCAGTGAGTFACTATAAAGCAAGAACCACTACTTCTTTGGGGAGGTAGGTCCTGCTTC
 -1120 CCTTCAACTCAGGATACAACTGCTTTCAAACGCTTTTCACTATTAGCTGACTAATTAGCTAGAAAGCCCTGTTCGTTAAACAA
 -1040 TTTTATGGTTGACTCCTTCCCTGGGCTCAGGGTTCCCTTAGAACACAGAGAGGTCCCCCAAATCCCGGTCCTGTGGCCCTGTCCCGC
 -960 CTAAGCTCTGCTCCCTGCCAGATCAGCAGGCAGCATTAGATTCTCATAGGAGCTGGACGCCCTATTGTTGAACCTGGGCATGT
 -880 GCGGGATCCAGATTGTGCACTCTTTATAGAAATCTAACTAATGCTTTGATGATCTATCTGNAACCAGAACAAATTTCAATCCCTG
 -800 AAACCATCCCCCACCAATCCATAGAAATACTGTCTTCCACAAAAATGATCCCTGGTGCCAAAAAATGTTAGAGACCACTCC
 -720 CCTAAAACTCTCTTCTTAGCTCTCACCTCCTGTATTACTATCTCATCTCAGTACATTGAAGCCCCCATCTTTTCCCCCATG
 -640 GATGCCCTCATTTCCCTATTAGGGAGGCATTTTATTATTTTTATTTTATTTTTCGGAGACGGAGTCTCGCTCTGTGCGC
 -560 CAAGGCTGGAGTGCAGTGGCGGATCTCGGCTCAGTGCAGACTCCGGCTCCCGGGTTACCGCCAATTTCTCCTGCTCAGGCC
 -480 TCCCAAGTAGCTGGGACTACAGGCGCCCGCACTACGCCCGGCTAAATTTTGTATTTTTGTATTTTTAGTAGAGACGGGGTTTTCACCG

Fig. 1A

-400 TGGTAGCCAGGATGGTCTCGATCTCCTGACCTCGTGATCCGCCCGCCCTTGGCCTCCCAAAGTGCTGGGATTACAGGCGGTG
 -320 AGACCGCGCCCGCGTCATTTGGTATGTCTTAATGTGCTCAGGACCTAGCACAGTCCCTGGTACCCAGTAGAGACCTA
 -240 TGTAAATGTTTCGTTATTCAATAAATACATGAATTAAGAGTGAGAGTGGATTTTGTAATGTTACGACTGATAGAGAGAAA
 -160 TACTCAGTGATTCTAAGGGATGGGGAAGAACGGTTGGAGCTAGAGGTTTGTGCTCAGGAAAACTATTAAATAGACGTTTCCCGC
 -80 AGGAAGGGATTGACGAAGTGTGAGGTTAATGAGGAAGGAAAAATAGAATATAAAATTTGGTGGTGGAAAAAGATCTGATTTTC
 •
 1 ATGATGCCGTGTCAGAGAGCAAAGCTCCTGTCCCTTTTGGCCCTAATTGGTGATGCTGTCTTTGGGTTCTTACCCACACCTCCT

-24 -20

↓

Met Val Met Gly Leu Gly Val Leu Leu Leu Val Phe
 +81 TTTTGGCCCTCCGCAGGAGCCTGTGTGGAAAGAG ATG GTG ATG GGC CTG GGC GTT TTG TTG TTG GTT TTC

-10

-1 +1

Val Leu Gly Leu Gly Leu Thr Pro Pro Thr Leu Ala Gln Asp Asn Ser Arg Tyr Thr His
 +144 GTG CTG GGT CTG GGT CTG ACC CCA CCG ACC CTG GCT CAG GAT AAC TCC AGG TAC ACA CAC

10

20

Phe Leu Thr Gln His Tyr Asp Ala Lys Pro Gln Gly Arg Asp Arg Tyr Cys Glu Ser
 +204 TTC CTG ACC CAG CAC TAT GAT GCC AAA CCA CAG GGC CCG GAT GAC AGA TAC TGT GAA AGC

Fig. 1B

30
 Ile Met Arg Arg Arg Gly Leu Thr Ser Pro Cys Lys Asp Ile Asn Thr Phe Ile His Gly
 +264 ATC ATG AGG AGA CGG GGC CTG ACC TCA CCC TGC AAA GAC ATC AAC ACA TTT ATT CAT GGC

 50
 Asn Lys Arg Ser Ile Lys Ala Ile Cys Glu Asn Lys Asn Gly Asn Pro His Arg Glu Asn
 +324 AAC AAG CGC AGC ATC AAG GCC ATC TGT GAA AAC AAG AAT GGA AAC CCT CAC AGA GAA AAC

 70
 Leu Arg Ile Ser Lys Ser Ser Phe Gln Val Thr Thr Cys Lys Leu His Gly Ser Pro
 +384 CTA AGA ATA AGC AAG TCT TCT TTC CAG GTC ACC ACT TGC AAG CTA CAT GGA GGT TCC CCC

 90
 Trp Pro Pro Cys Gln Tyr Arg Ala Thr Ala Gly Phe Arg Asn Val Val Ala Cys Glu
 +444 TGG CCT CCA TGC CAG TAC CGA GCC ACA GCG GGG TTC AGA AAC GGT GTT GCT TGT GAA

 110
 Asn Gly Leu Pro Val His Leu Asp Gln Ser Ile Phe Arg Arg Pro Stop
 +504 AAT GGC TTA CCT GTC CAC TTG GAT CAG TCA ATT TTC CGT CGT CCG TAA

 CCAGCGGGCCCTGGTCAAGTGCTGGCTCTTGCTGTCTTGCCTTCCATTTCGCCCTCTGCA
 +552
 CCCAGAACAGTGGTGGCAACATTTCATTGCCAAGGGCCCCAAGAAAGAGCTACCTGGACCTTTTGTCTTCTGTGTGACAAC
 +612
 ATGTTTAATAAAATAAAATGTCTTGATATCAGTAAGAAATCAGAGTCTTCTCAGCTGATTTCTGGGCATATTGATCTTTCGCC
 +692
 CATTTCCTACTTGGCTGCTCCCTGAGAGGACTGCATAGGATAGAAAATGCCCTTTTCTTTTCTTTTCTCGTTTTTTTTT
 +782

Fig. 1C

+862 TTT TTT TTT TGGATGGAGTCTCAC TCTGTGCGCCAGGCTTAA GTGCAATGGCA CAATCTCGGCTCAC TGGCAACCTCTCT
 +942 CTCCTGGGTTC AAGTGAT TCTCCTGCC TCAGCC TCCCAAA TAGCTGAGATTA CAGGCATGCA CCAACACACCTGGCTAAT
 +1022 TTT TGTGT TTTTAGTAGACAGAGGTTC ACCGTTT TGGCCAGGT TGGTCTT TGAAC TCTGACCTCGGGAGATCGGCCCA
 +1102 CC TGGCCTCTCT TTTGTGCTGGGATTA CAGGCATGAGCCACTGAGCCGGCCACTTTT TCCCTTAATCAGTTCAGT TTTTACA
 +1182 AGTCATTAGGGAGGTAGACTTTTACCTCTCTGTGAAGGAAAGTATGGTATGT TGTATCTTACAGAGAGAGATGGAAAAATTC
 +1262 AGGGCTCGTAGCTACTAAGCAGAA TTTCCAAGATAGGCAAA TTTGTTTTTTCTGTCAAATAA TTAAGCTTAATA TTACTTCTTA
 +1342 CAATA TGAGACCTTGGAGAGAGT TTTCCAAGGACCAAGTACCAACA TACCAACAGATTAATTA TAGTTTCTCTCACACTCTT
 +1422 ACACACACACACATATACACATATGTAA TCCAGCATGAATACCAAA TTTCA TCAAGGTAGCCACCTTTTGTCTTTA
 +1502 ATCGAGAGATAA TTTTGATGTTTGAA TGGAA TGTCTCCAGGATATCTCTTTGTCTATGGT TAA TTTTATATAAAA TTTCAAAA
 +1582 ACCAATTA CATTA TTTCCCTCTGTAA TCTTTTACTTTTATCAACTAATGTCTGGCAAGTGTGA TGT TTTGGGGAAGTTTATAG
 +1662 AAGATTTCCGGCCAGGCGCTTATCTCACGCTTGTAA TCCAGCACTTTGGGAAGCTGAGCGCGACAGATCACGAGGTCAAGA
 +1742 GATCAAGACCATCTGGACAACATGGTGAAACCTTGTCTCTACTA AAAATGTGAAAA TTAGCTGGGCGTGGTGGCACACA
 +1822 CCTATAGTCCCAGCTACTCGGGAGGCTGAGGCAGGAGAA TCGCTTGAACCTTAGGAGCGGAGGTTCACCTGAGCCGAGAT
 +1902 CACGCCACTGC ACTCCAGCCTGGCGCACAGAGCGAGACTCCATCTCMAAAAAA AAAAAAGAAAGATCCCAGTTTATTC
 +1982 CCAGTTTATCCCC TATTTCTTCC TCAATTTCTCAAGATTTGT TTTTAAAGTTAA CATAA CTTAGGTTAACACACACTCTTTGTAA
 +2062 AATACACTGTTCAATCTACAGACTCAGTGGTTAGCTTCC TGTTAAC TAAATTTCTGTGACAGGTACTTTGGATATTTTAT

Fig. 1D

+2142 TAGAAAGTGGTTGCCCAATAAATTAGTTATAAGTCGCCAGTTTCACTGCCCTTGTGAACACATTAATTAATGTGGTCTCAGTA
 +2222 TTCCCTATGGTGGCTTCTCCTGCTCCTGCTATTTGCCCTGAAATGGGCCCAAAAGCCGTGGCTCCCCAATGCTCAGGTTATA
 +2302 GAAACATTTCCAGGTACCACTTAGGAGAGCCCAGCCTCACITGAAAAGTATTCAAATTTAGGAATGGGTTTGAGAAAGTAGGT
 +2382 AGCTGGTATGTGCTTAGCACAAAGAACTCTCTCTTCCCTTGGGTAGTCTGTCTTCAAAAACCTGAAAAACACTGTCTCATTTCCCTTAAG
 +2462 AAAATAGGAAAAAGTATTTCCAAAACCTCTGTCACTAGAAAAATTTGCCAATATTAACCAAAATCTCAAAAACCTCTCAGGAAATG
 +2542 AGAAAGTCCCAGTTTCTGGTAAACATATTTGGGCCCTTTTCTCAAGTTTCTCCTTCCAGTGCCTATTTTCCCTTGAGGTGAGGCA
 +2622 AAGTTACTCAAGATCATCGCTGCCACTCAAGGCCCTTGATAGGGCAAGTGAAAAGGCAATGCATCGCATAGTTTGGCTCTGGTGTTCAGG
 +2702 GCATAAGCTGTGAAAAACCCACATCTTCTCCAAACATCTGCTTGGAGCATTATCATCGCATAGTTTGGCTCTGGTGTTCAGG
 +2782 GAAATCGCTGTTTCATAGGAAATCACATGGCAGTGGGAGTGTTTTCCCTGACCITGCCGATGGTACCTGGCACCTGAGC
 +2862 AAGCATTCCTAGTCCTTTTTTGGTCTGGGCCCTCTTGTCTATCACAAACCACAAGCTGTTTAAANAAAAACGTCAAAGTCAC
 +2942 AGGCAGGTCAATTTTATCCTGCGTGAATCAATTTGAAG

Fig. 1E

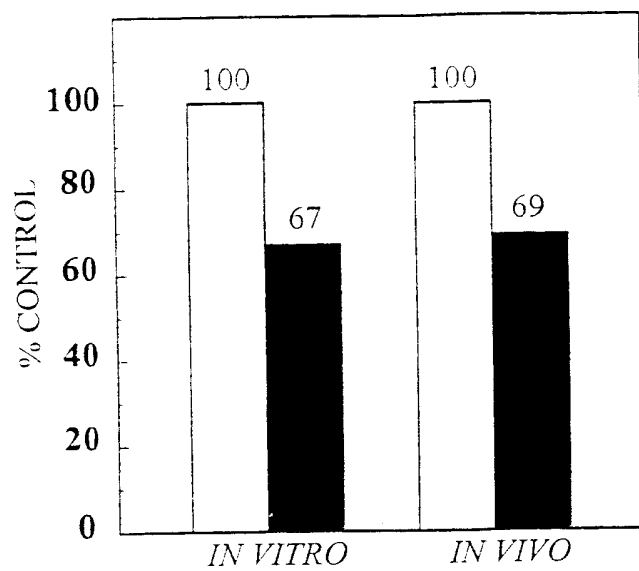


Fig. 2A

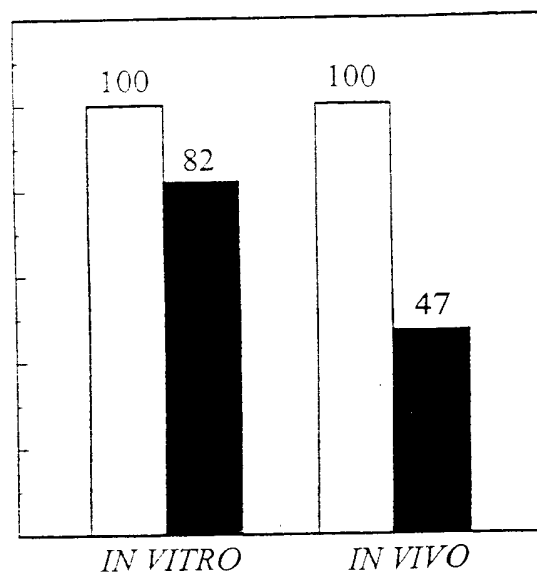


Fig. 2B

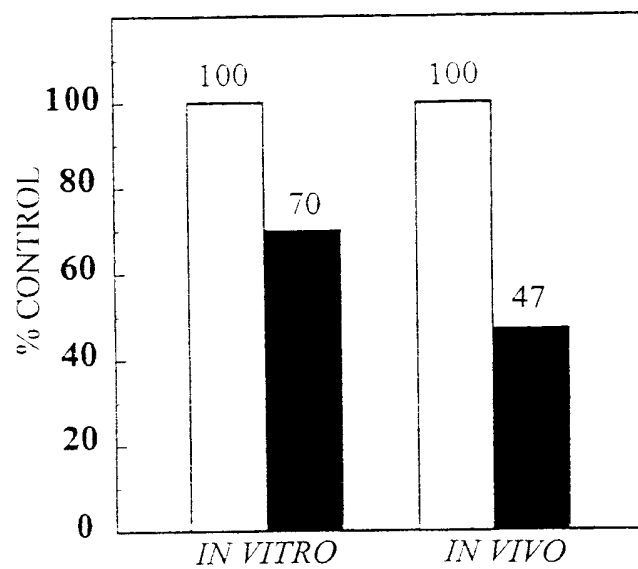


Fig. 3A

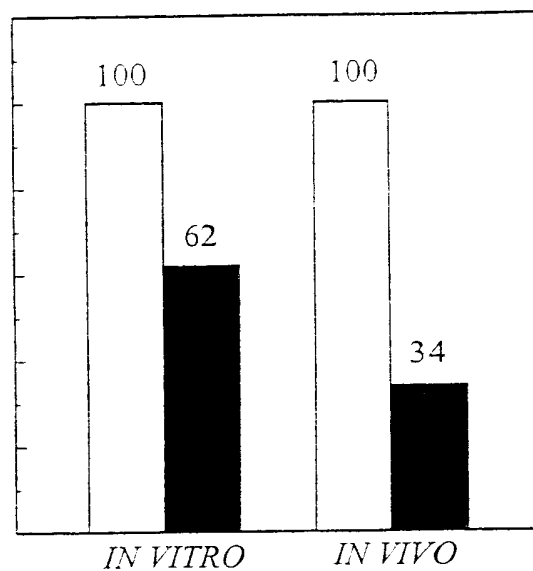


Fig. 3B

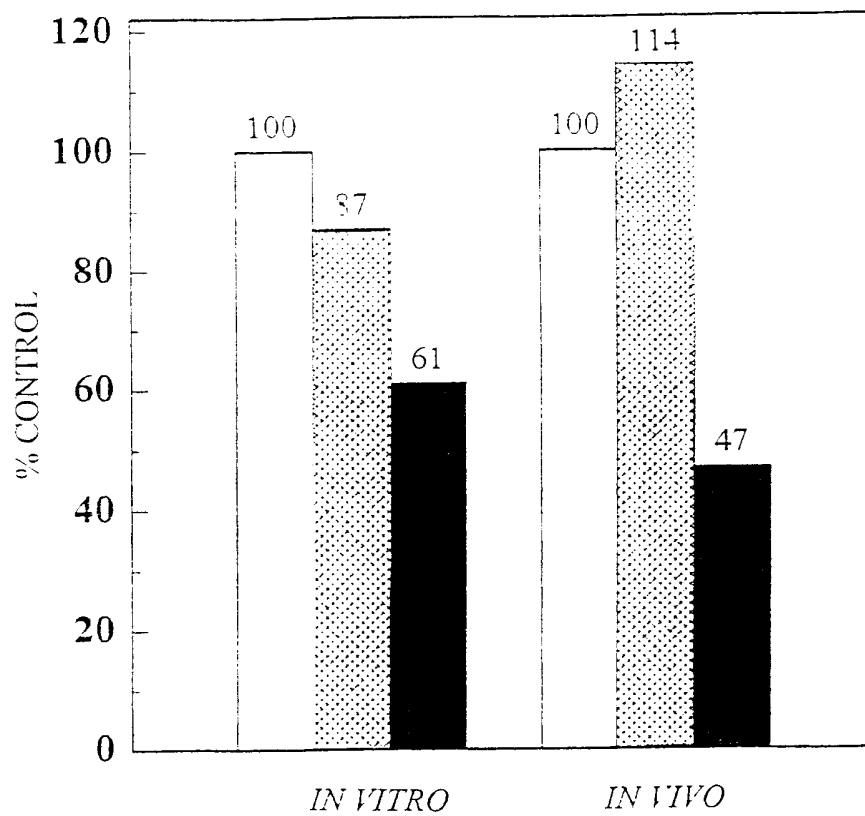


Fig. 4

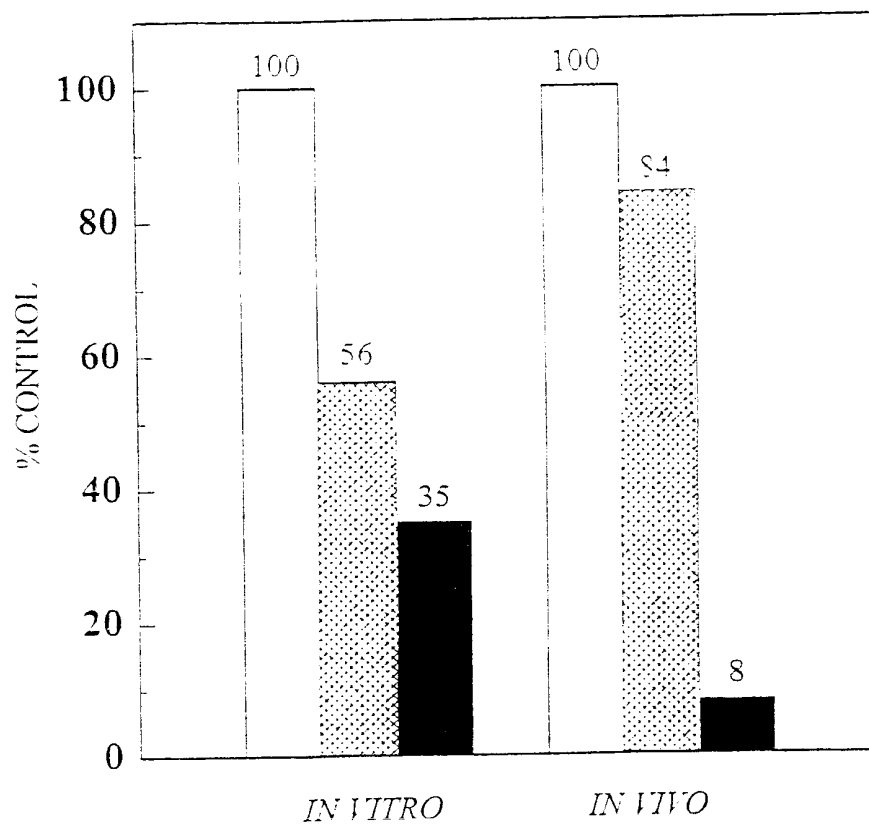


Fig. 5

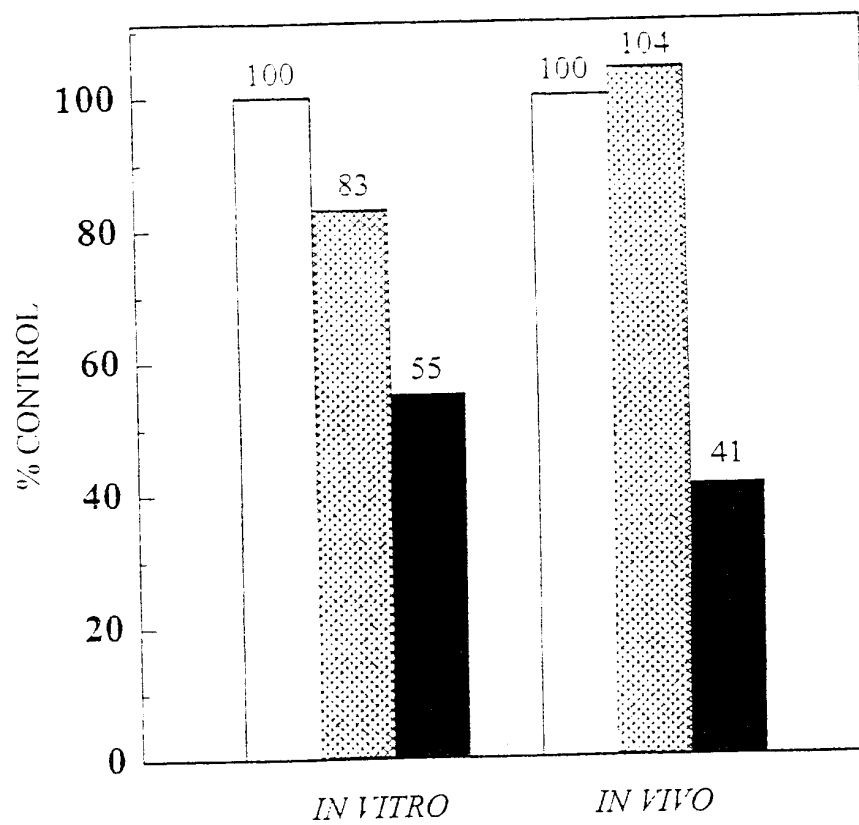


Fig. 6

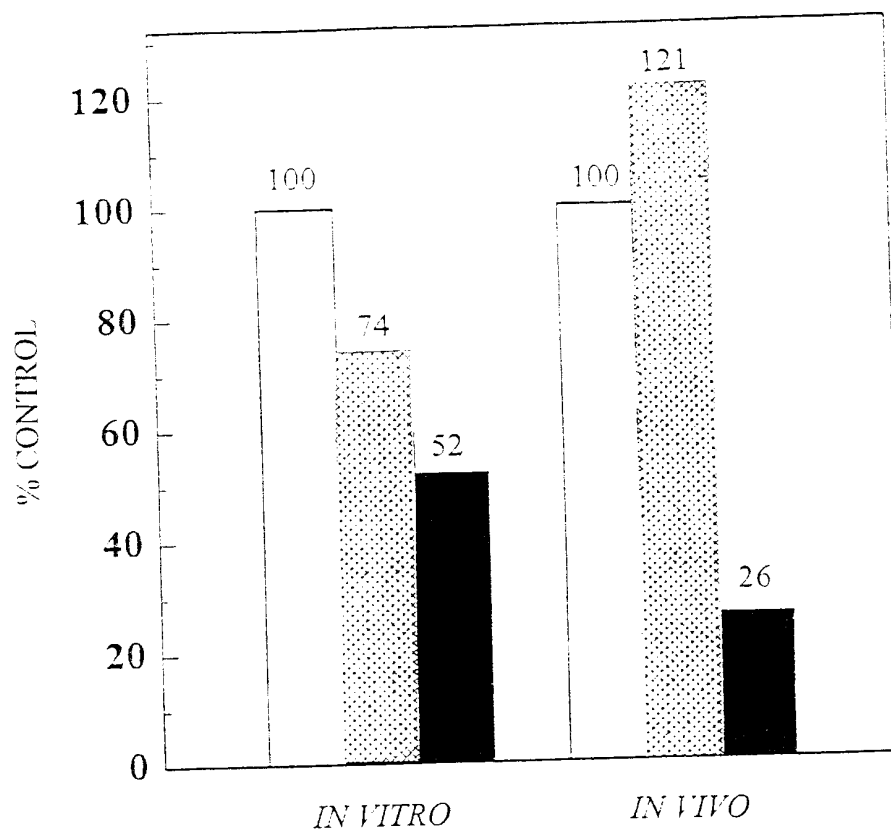


Fig. 7

FIG. 8



FIG. 9

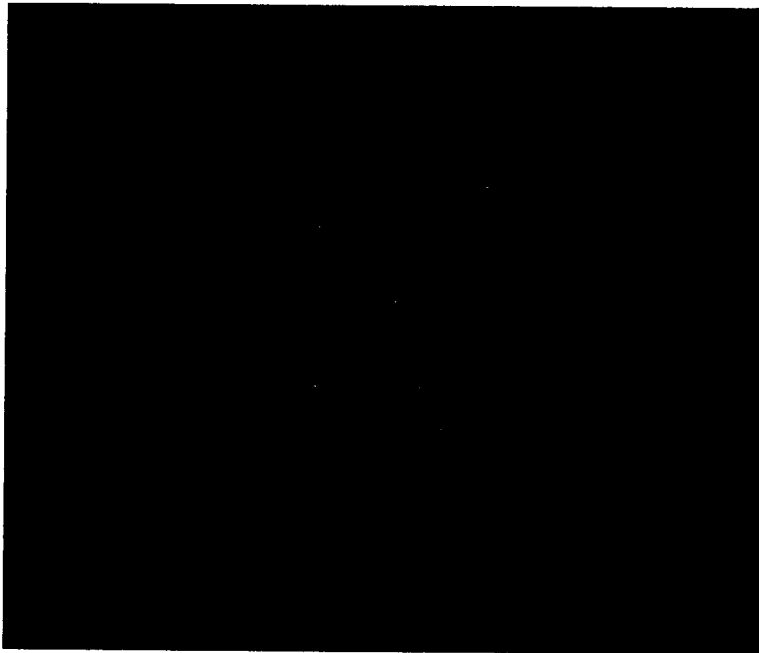


FIG. 10

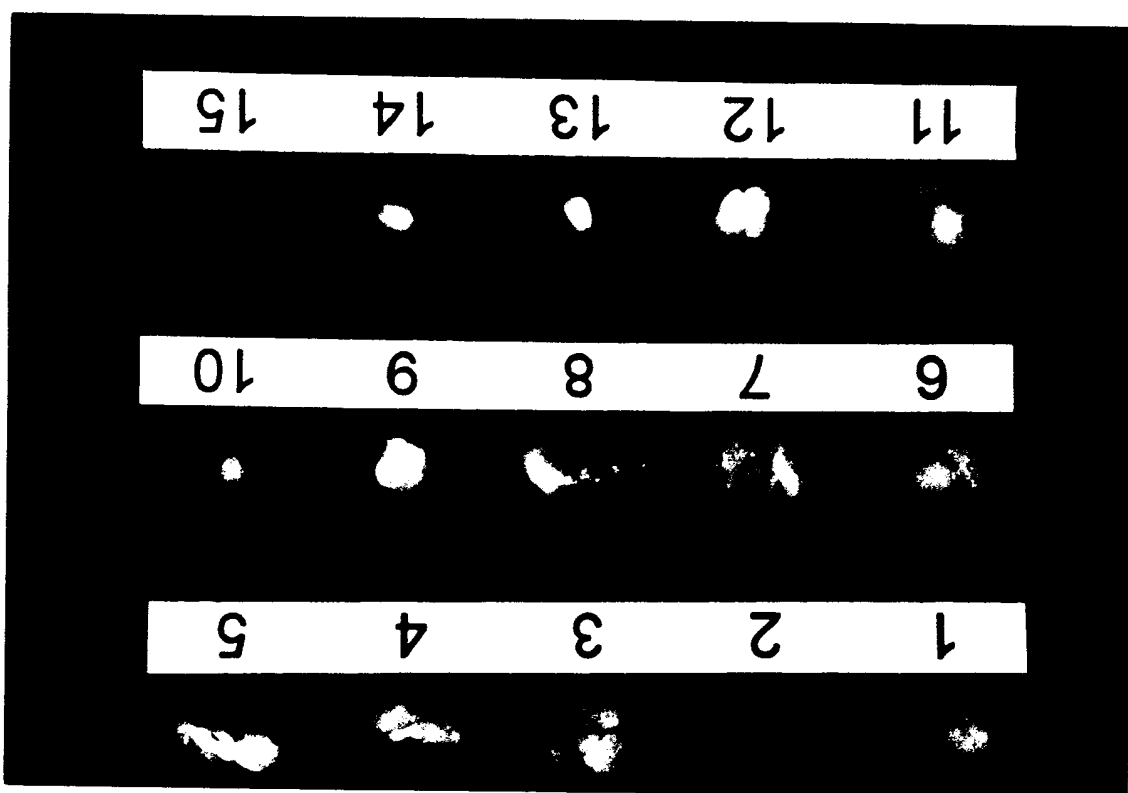


FIG. 11

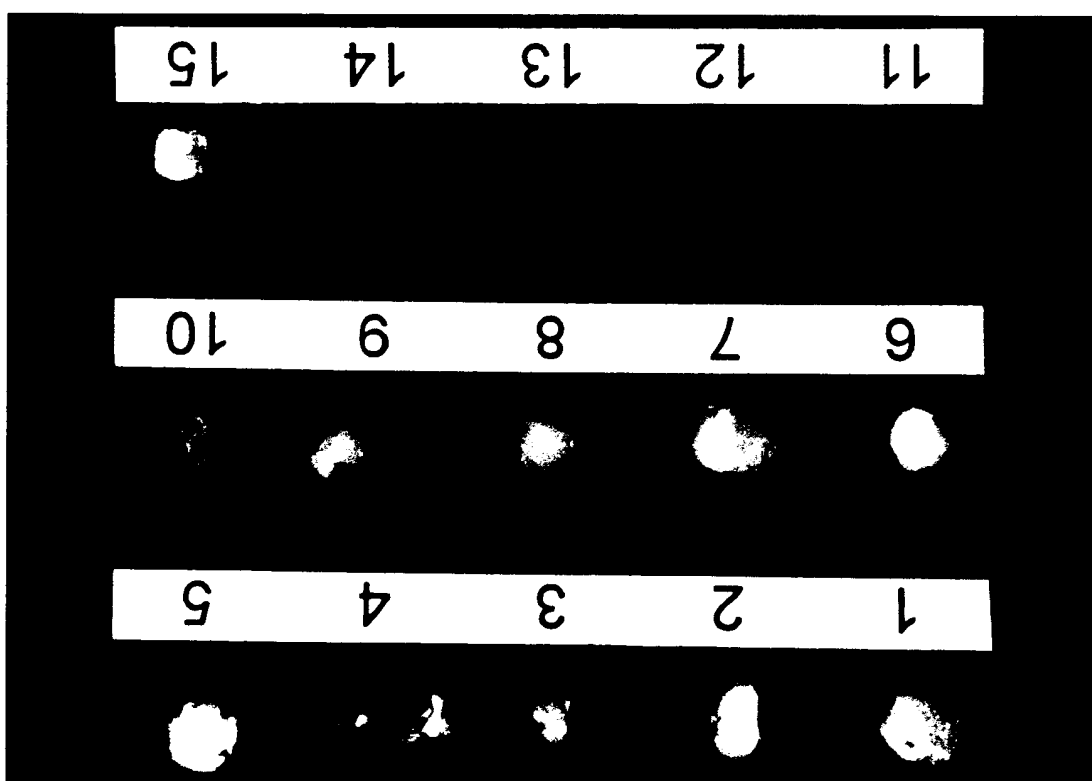


FIG. 12

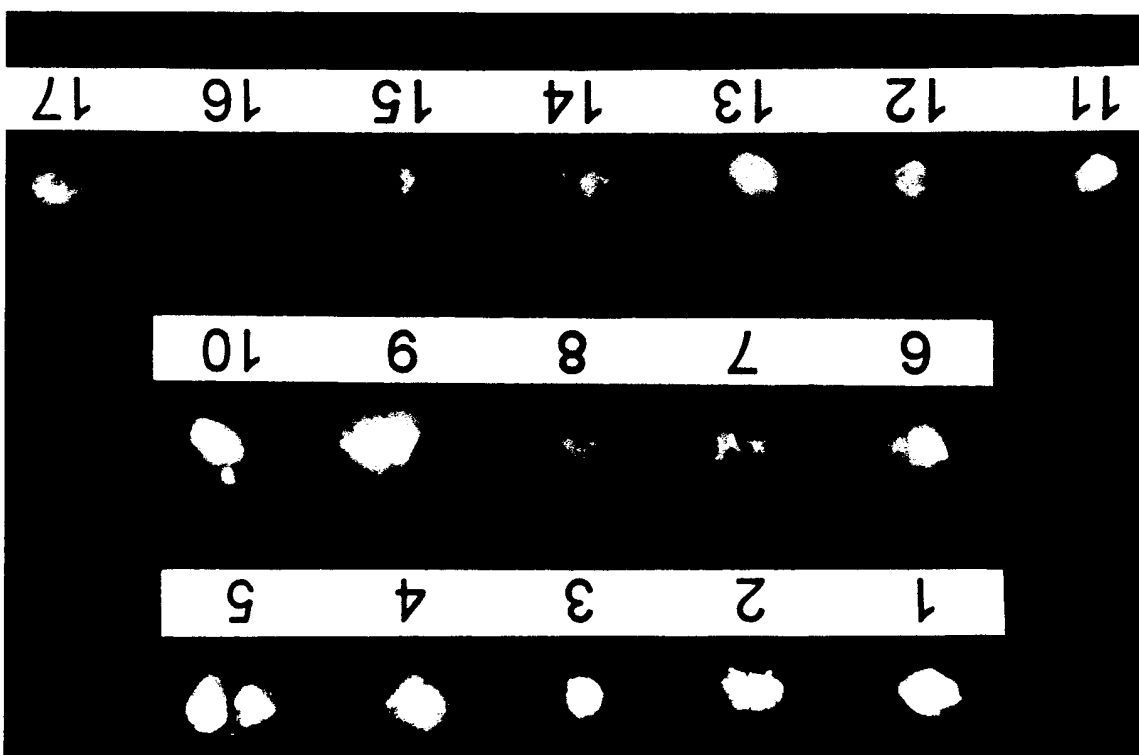
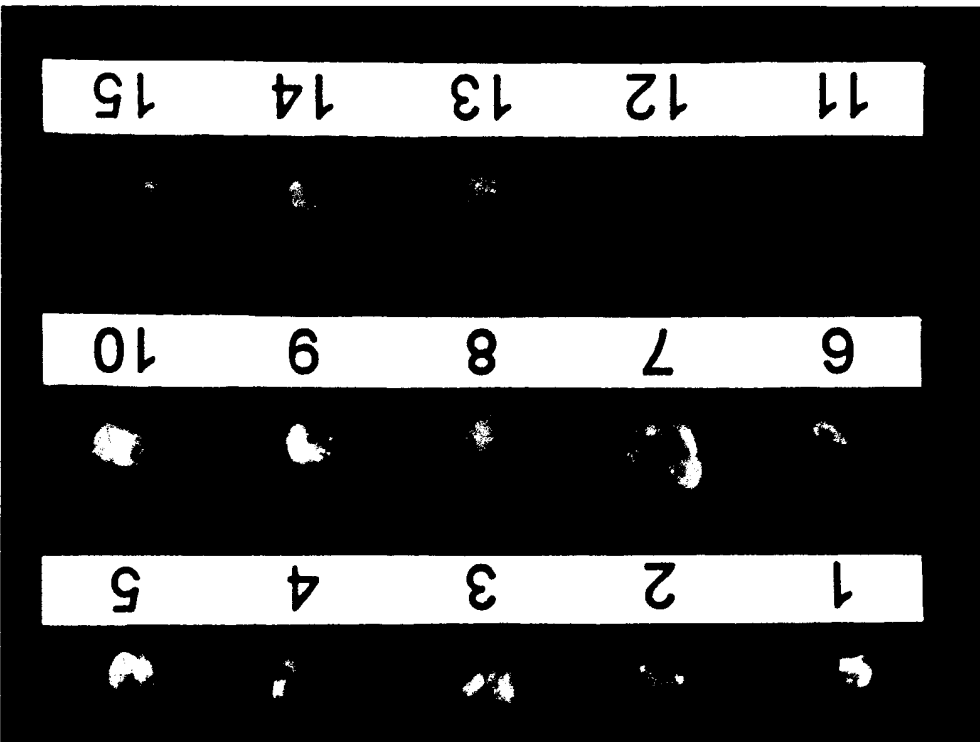
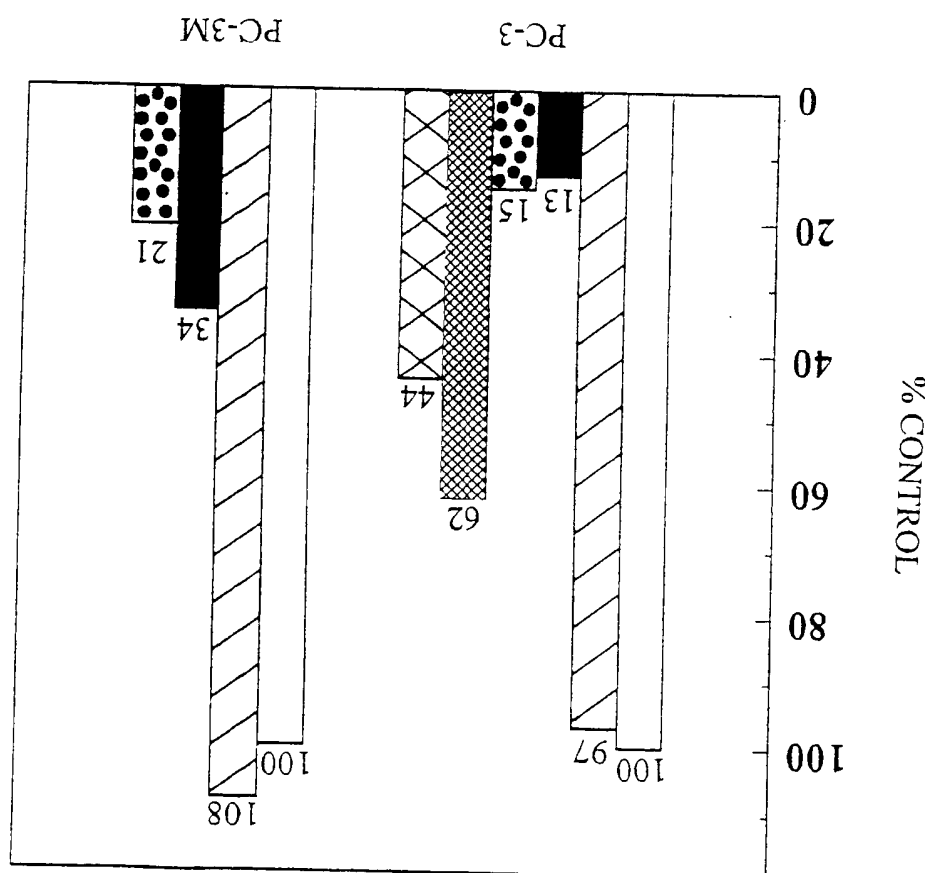


FIG. 13



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74. 14



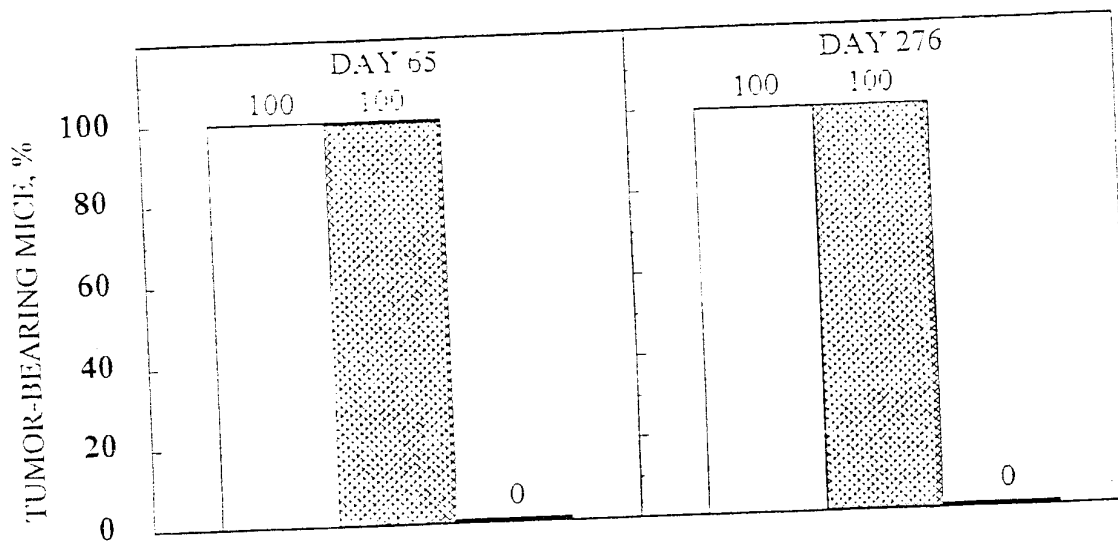


Fig. 15A

Fig. 15B

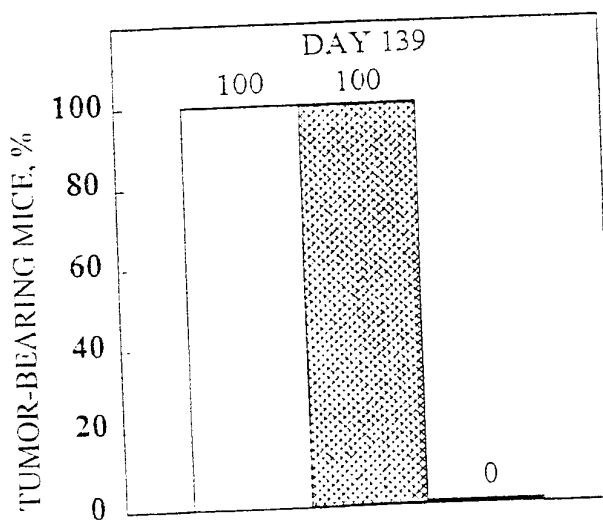


Fig. 15C

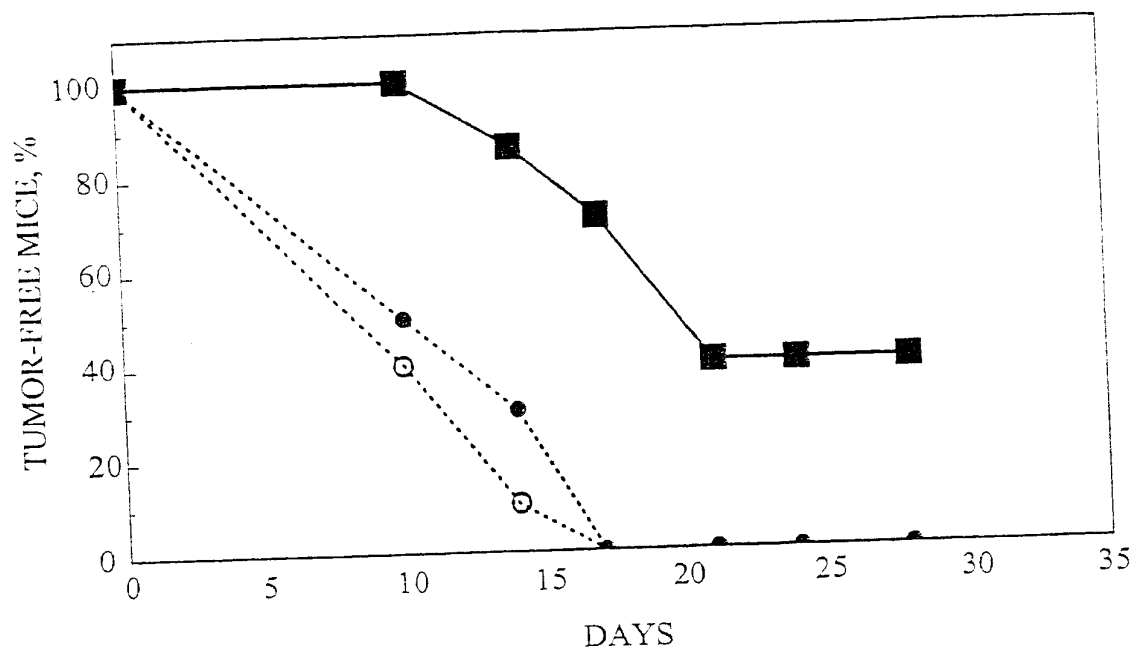


Fig. 16

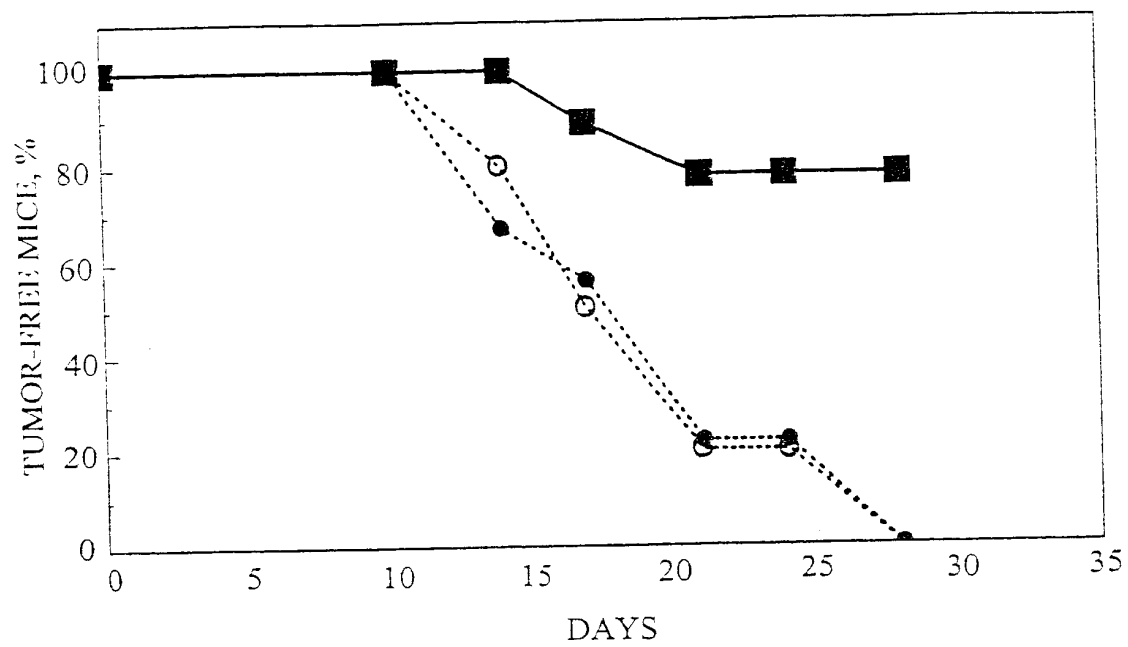


Fig. 17